Claims

1. A pharmaceutical composition comprising lercanidipine or an analog or a pharmaceutically acceptable salt thereof as an active substance and a pharmaceutically acceptable vehicle, which composition upon oral administration to a mammal in need thereof releases the active substance in a controlled manner.

2. A pharmaceutical composition according to claim 1, wherein the active ingredient is fully dissolved in the vehicle to form a solid solution at ambient temperature.

3. A pharmaceutical composition according to claim 1, wherein the active ingredient is partly dissolved in the vehicle to form a mixture of solid dispersion and solid solution at ambient temperature.

4. A pharmaceutical composition according to claim 1, wherein the active ingredient is dispersed in the vehicle to form a liquid suspension or solid dispersion at ambient temperature.

5. A pharmaceutical composition according to claim 4, wherein the vehicle has a melting point between about 20°C and about 250°C.

6. A pharmaceutical composition according to claim 1, wherein the vehicle is hydrophobic and may be selected from the group consisting of straight chain saturated hydrocarbons, paraffins; fats and oils such as cacao butter, beef tallow, lard; higher fatty acid such as stearic acid, myristic acid, palmitic acid; hydrogenated tallow, substituted and/or unsubstituted triglycerides, yellow beeswax, white beeswax, carnauba wax, castor wax, japan wax, and mixtures thereof.

7. A pharmaceutical composition according to claim 1, wherein the vehicle is a water-miscible polar lipid preferably selected from the group consisting of sorbitan esters, polyether glycol esters; higher alcohols such as cetanol, stearyl alcohol; glyceryl monooleate, substituted and/or unsubstituted monoglycerides, substituted and/or unsubstituted diglycerides, and mixtures thereof.

8. A pharmaceutical composition according to claim 1, wherein the vehicle is hydrophilic or water-miscible and is selected from the group consisting of polyethylene glycols,

polyoxyethylene oxides, poloxamers, polyoxyethylene stearates, poly-epsilon caprolactone and mixtures thereof.

9. A pharmaceutical composition according to claim 1, wherein the vehicle is hydrophilic or water-miscible and is selected from the group consisting of polyvinylpyrrolidones, polyvinyl-polyvinylacetate copolymers (PVP-PVA), polyvinyl alcohol (PVA), PVP polymers, acrylic polymers, polymethacrylic polymers (Eudragit RS; Eudragit RL, Eudragit NE, Eudragit E), myristyl alcohol, cellulose derivatives including hydroxypropyl methylcellulose (HPMC), hydroxypropyl cellulose (HPC), methylcellulose, sodium carboxymethylcellulose, hydroxyethyl cellulose, pectins, cyclodextrins, galactomannans, alginates, carragenates, xanthan gums and mixtures thereof.

10. A pharmaceutical composition according to claim 1, wherein the vehicle is hydrophilic or water-miscible vehicle and is selected among polyglycolized glycerides such as Gelucire®.

11. A pharmaceutical composition according to claim 10, wherein the vehicle is Gelucire® 44/14.

12. A pharmaceutical composition according to claim 7, wherein the vehicle is selected among glyceryl monolaurate, glyceryl monocaprylate and glyceryl (mono)caprate.

13. A pharmaceutical composition according to claim 1 in the form of particles, i.e. in particulate form.

14. A pharmaceutical composition according to claim 1, wherein the concentration of active substance in the vehicle is less than about 30w/w%, based on the total weight of the active substance and the vehicle.

15. A pharmaceutical composition according to claim 1, wherein the concentration of active substance in the vehicle is at least about 1w/w%, based on the total weight of the active substance and the vehicle.

16. A solid dosage form comprising the pharmaceutical composition according to claim 1 and one or more pharmaceutically acceptable excipients.

17. A solid dosage form according to claim 16, which provides an AUC value relative to that of commercially available Zanidip® tablets of at least about 1.1, or at least about 1.2, or at

least about 1.3, or at least about 1.4, or at least about 1.5, or at least about 1.75 or more, or at least about 2.0, or at least about 2.5, or at least about 3.0, the AUC values being determined under similar conditions.

18. A solid dosage form according to claim 16, which provides a c_{max} value relative to that of commercially available Zanidip® tablets of at least about 1.1, or at least about 1.2, or at least about 1.3, or at least about 1.4, or at least about 1.5, or at least about 1.6 or more, or at least about 2.0, or at least about 2.5, or at least about 3.0, the c_{max} values being determined under similar conditions.

19. A solid dosage form according to claim 16 in the form of tablets, beads, capsules, grains, pills, granulates, granules, powder, pellets, sachets or troches.

20. A solid dosage form according to claim 19, which is a tablet.

21. A solid dosage form according to claim 19, which is a capsule.

22. A solid dosage form according to claim 16, which is which is a unit dosage form for oral, buccal or sublingual administration.

23. A solid dosage form according to claim 16, wherein the pharmaceutically acceptable excipient is selected from the group consisting of fillers, disintegrants, binders, diluents, lubricants and glidants.

24. A solid dosage form according to claim 16, which further comprises a pharmaceutically acceptable additive selected from the group consisting of flavoring agents, coloring agents, taste-masking agents, pH-adjusting agents, buffering agents, preservatives, stabilizing agents, anti-oxidants, wetting agents, humidity-adjusting agents, surface-active agents, suspending agents, absorption enhancing agents.

25. A solid dosage form according to claim 16 comprising at least one pharmaceutically acceptable excipient selected from the group consisting of silica acid and derivatives or salts thereof including silicates, silicon dioxide and polymers thereof; magnesium aluminosilicate and magnesium aluminometasilicate, bentonite, kaolin, magnesium trisilicate, montmorillonite and saponite.

26. A solid dosage form according to claim 25 comprising a silica acid or a derivative or salt thereof.

27. A solid dosage form according to claim 25 comprising silicon dioxide or a polymer thereof.

28. A solid dosage form according to claim 25 comprising magnesium aluminosilicate.

29. A solid dosage form according to claim 16, which comprises an oily material.

30. A solid dosage form according to claim 29, wherein the concentration of the oily material in the dosage form is about 5% w/w or more such as, e.g., about 10% w/w or more, about 15% w/w or more, about 20% w/w or more, about 25% w/w or more, about 30% w/w or more, about 35% w/w or more, about 40% w/w or more, about 45% w/w or more, about 50 w/w or more, about 55% w/w or more, about 60% w/w or more, about 65% w/w or more, about 70% w/w or more, about 75% w/w or more, about 80% w/w or more, about 85% w/w or more, about 90% w/w or more or about 95% w/w or more.

31. A solid dosage form according to claim 16, which upon oral administration to a mammal in need thereof releases the active substance in a controlled manner.

32. A solid dosage form according to claim 31, which does not exhibit a significant adverse food effect as evidenced by a value of (AUC_{fed}/AUC_{fasted}) of at least about 0.85 with a lower 90% confidence limit of at least 0.75.

33. A solid dosage form according to claim 32, wherein the value of (AUC_{fed}/AUC_{fasted}) is at the most about 3, such as, e.g. at the most about 2.5, at the most about 2.0, at the most about 1.5, at the most about 1, such as, e.g., about 0.9 or more, about 0.95 or more, about 0.97 or more or about 1 or more.

34. A solid dosage form according to claim 16, which upon oral administration to a mammal in need thereof releases the active substance in a controlled manner and reduces inter- and/or intra-individual variations compared to those of Zanidip® administered under the same conditions and in a dose that provides an equivalent therapeutic effect.

35. A solid dosage form according to claim 16, which releases at least about 20% w/w of the total amount of the active substance within about 8 hours, within about 6 hours, within about

4 hours, within about 3 hours or within about 2 hours, when tested *in vitro* according to the USP II dissolution test (paddle) using 0.3% polysorbate 80 in 0.1N HCl as medium, 100 rpm.

36. A solid dosage form according to claim 16, which releases at least about 40% w/w of the total amount of the active substance within about 10 hours such as, e.g., within about 8 hours, within about 7 hours, within about 6 hours, within about 4 hours or within about 3 hours, when tested *in vitro* according to the USP II dissolution test (paddle) using 0.3% polysorbate 80 in 0.1N HCl as medium, 100 rpm.

37. A solid dosage form according to claim 16, which releases at least about 55% w/w such as, e.g., about 60% w/w or more, about 65% w/w or more, about 70% w/w or more, about 75% w/w or more or about 80% w/w or more of the total amount of the active substance within about 24 hours such as, e.g., within about 16 hours, within about 12 hours, within 10 hours, within 9 hours, within about 8 hours, or within about 6 hours, when tested *in vitro* according to the USP II dissolution test (paddle) using 0.3% polysorbate 80 in 0.1N HCl as medium, 100 rpm.

38. A solid dosage form according to claim 16, which upon oral administration to a mammal in need thereof in a controlled manner releases at least about 20% w/w of the total amount of the active substance within about 8 hours, within about 6 hours, within about 4 hours, within about 3 hours or within about 2 hours.

39. A solid dosage form according to claim 16, which the composition upon oral administration to a mammal in need thereof releases at least about 40% w/w of the total amount of the active substance within about 16 hours such as, e.g., within about 12 hours, within about 10 hours, within about 8 hours, within about 7 hours, within about 6 hours, within about 4 hours or within about 3 hours.

40. A solid dosage form according to claim 16, which upon oral administration to a mammal in need thereof releases at least about 55% w/w such as, e.g., about 60% w/w or more, about 65% w/w or more, about 70% w/w or more, about 75% w/w or more or about 80% w/w or more of the total amount of the active substance within about 24 hours such as, e.g., within about 16 hours, within about 12 hours, within 10 hours, within 9 hours, within about 8 hours, or within about 6 hours.

41. A solid dosage form according to claim 16, wherein the concentration of the pharmaceutical composition is in a range of from about 5% to 100% w/w such as, e.g., from

about 10% to about 90% w/w, from about 15% to about 85% w/w, from about 20% to about 80% w/w, from about 25% to about 80% w/w, from about 30% to about 80% w/w, from about 35% to about 80% w/w, from about 40% to about 75% w/w, from about 45% to about 75% w/w or from about 50% to about 70% w/w of the dosage form.

42. A solid dosage form according to claim 41, wherein the concentration of the pharmaceutical composition in particulate form is about 50% w/w or more of the dosage form.

43. A solid dosage form according to claim 16, wherein the solid dosage form upon oral administration to a mammal in need thereof releases lercanidipine in a controlled manner and the solid dosage form being essentially bioequivalent with Zanidip® or a similar commercially available lercanidipine-containing product.

44. A solid dosage form according to claim 43, wherein the dosage form is administered in a dose that is at the most about 85% w/w of the dose of lercanidipine administered in the form of Zanidip® or a similar commercially available lercanidipine containing product.

45. A method of manufacturing the solid oral dosage form of claim 16 comprising the steps of:

i) Bringing the vehicle in liquid form to obtain a liquid vehicle,

ii) Maintaining the liquid vehicle at a temperature below the melting point of the active substance,

iii) Dissolving the desired amount of active substance in the vehicle of i),

iv) Spraying the resulting solution onto a solid carrier having a temperature below the melting point of the vehicle to obtain a composition,

v) Mechanically working the resulting composition to obtain particles, i.e. a particulate material, and

vi) Optionally subjecting the particulate material to conventional methods for preparing solid dosage forms.

46. A method of manufacturing the solid oral dosage form of claim 16 comprising the steps of:

i) Bringing the vehicle in liquid form to obtain a liquid vehicle,

ii) Suspending the desired amount of active substance in the vehicle of i),

iii) Spraying the resulting suspension or dispersion onto a solid carrier having a temperature below the melting point of the vehicle to obtain a composition,

iv) Mechanically working the resulting composition to obtain particles, i.e. a particulate material, and

v) Optionally subjecting the particulate material to conventional methods for preparing solid dosage forms.

47. Use of the composition according to claim 1 to enhance the oral bioavailability of lercanidipine or an analog or pharmaceutically acceptable salt thereof.

48. Use of the composition according to claim 1 for the preparation of a delayed release oral solid dosage form, preferably tablets or capsules.